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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/002,974	10/26/2001	Gabriel Nunez	UM-06646	3481

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EXAMINER	
GOLDBERG, JEANINE ANNE	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 04/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/002,974	NUNEZ ET AL.	
	Examiner	Art Unit	
	Jeanine A Goldberg	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,7,11,12,24-27,33,38 and 39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,7,11,12,24-27,33,38 and 39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to the papers filed February 13, 2004. Currently, claims 1, 3-4, 7, 11-12, 24-27, 33, 38-39 are pending.

2. Any objections and rejections not reiterated below are hereby withdrawn.

Specification

3. A new Figure 33 has been provided which corrects the numbering after 3122. It is noted that the figure previously contained 11 nucleotides in a 10 nucleotide segment, thereby setting the numbering system off by 1 nucleotide.

4. Upon close comparison of SEQ ID NO: 1 and 33, the sequences appears to differ in an insertion of a C at location 3124 of SEQ ID NO: 33. This does not appear to correspond to the specification which teaches a mutation at 3020 (Table 1, page 64). Although the specification does not specifically teach an insertion of a C at location 3124 of SEQ ID NO: 33, the specification does clearly provide SNP sequences in Figure 26 which provides primers or probes to the SNP region. This region only corresponds to position 3124 of SEQ ID NO: 33, not position 3020. The Figure also states that the numbering system is relative to Ogura which when compared to SEQ ID NO: 33, aligns to position 3124 of SEQ ID NO: 33. Therefore, a cytosine insertion at position 3124 of SEQ ID NO: 1 is not considered new matter in view of the foregoing remarks.

Priority

5. This application claims priority to provisional applications 60/244,266, filed October 30, 2000 and 60/286,316, filed April 25, 2001.

It is noted that the provisional filed in October 30, 2000 only appears to teach a single variation within the scope of the claims, namely an insertion of C which results in the truncation of the protein. However, it is not until April 25, 2001 that the specification appears to enable the use of an insertion of C as associated with Crohn's disease by providing statistical values for the population studies.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 24-27, 33, 39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of determining an individual patient's risk by determining the presence of a variant at position 3124 of SEQ ID NO: 1 and delivering the results from the assay to the use via a computer or internet, does not reasonably provide enablement for a method for calculating a patients risk with software. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention and breadth of claims

Claims 24-27, 33, 39 are drawn to a computer implemented method of determining a patient's risk of developing Crohn's disease by entering the genetic variation information into the computer and calculating the patient's risk with said software. The invention is an class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The unpredictability of the art and the state of the prior art and Guidance in the Specification

The specification discusses bioinfomatics methods and discusses computers storing genetics data. The specification also discusses delivering results to the user via a computer or the internet. The specification, however, fails to provide any particular software package or a developed software package for calculating or predicting a patients risk of developing Crohn's disease with software.

The guidance provided by the specification amounts to an invitation for the skilled artisan to try and follow the disclosed instructions to make and use the claimed invention. The specification merely discloses the idea of automating the method, but fails to provide any software program. The specification does not teach any software which calculates relative risk or population attributable risk. Moreover, there is no software which uses additional risk factors to determine such risks.

Working Examples

The specification has no working examples of a software for predicting a patient's risk of developing Crohn's disease.

Quantity of Experimentation

The quantity of experimentation in this area is extremely large since there is significant number of parameters which would have to be studied to develop a computer software program for the prediction of a patient's risk of developing Crohn's diseases. The software program could be broadly drawn to inputting age, sex, family history etc to enable prediction of patient's risk of Crohn's disease. The claim is not particularly limited in any way. It is further unclear whether the claim is directed to a value of risk or whether the claim is drawn to a yes/no answer for increased risk. Moreover, the claim appears to take the genetic material from a patient, perform a nucleic acid based wet assay on the material and place the information from the laboratory results into the computer. The specification does not teach any particular software for obtaining risk information in the Nod2 gene and Crohn's disease. The specification appears to contemplate delivery of the results via the computer or the internet, however this is not software that calculates any particular association or risk. The software contemplated

by the instant claims appears to be more than just results. There is no software taught in the art or in the instant specification for prediction of risk of Crohn's disease. This would require inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps.

Level of Skill in the Art

The level of skill in the art is deemed to be high.

Conclusion

In the instant case, as discussed above, in a highly unpredictable art where the specification fails to provide specific guidance as to the software program and its design, it is undue experimentation to design a computer program to evaluate the method claimed in the instant specification. Further, the specification provides insufficient guidance to overcome the art recognized. Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the absence of a working example and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1, 3-4, 7, 11-12, 24-27, 33, 38-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1, 3-4, 7, 11-12, 38 are indefinite because it is unclear how the skilled artisan would identify a risk of developing Crohn's disease. The claim as written appears to indicate that the detection of either the presence or absence of the insertion C identifies subjects at risk of developing Crohn's disease. The specification does not support this. Rather the specification teaches that the insertion is indicative of an increased risk. The mere detection of the presence or absence of a variant does not identify subjects at risk of developing Crohn's disease. The rejection may be easily overcome by amending the claim to recite:

1. A method of detecting an increased risk of an subject for developing Crohn's disease comprising

a) providing a nucleic acid from a subject, wherein said nucleic acid comprises a Nod2 gene; and

b) detecting the presence or absence of a variant Nod2 gene, wherein said variant Nod2 gene has a nucleic acid sequence having a cytosine insertion at position 3124 of SEQ ID NO: 1

wherein the presence of a cytosine insertion at position 3124 of SEQ ID NO: 1 is indicative of the subject to having an increased risk to Crohn's disease.

B) Claims 3-4 are indefinite because it is unclear what a genotype relative risk for said subjects encompasses. The specification teaches that the difference between

the frequency of the mutation in a diseased and control population is significantly different. The specification also teaches the presence of homozygous and heterozygous. Therefore, it is unclear how the method is further defined by the genotype relative risk since the specification teaches this and the method is for identifying Crohn's disease. Similarly, Claim 4 is related to population attributable risk. The claim appears as though is may no longer be appropriate for the instant claim set, but was rather appropriate for an undetermined variant that was yet to be discovered, which is no longer encompassed by the instant claim.

C) Claim 7 is indefinite because it is unclear whether Claim 7 further limits Claim 1. The variation inherently results in increased NF-kB activation. Moreover, it is unclear how this Claim modifies and limits Claim 1 directed to a method of identifying subjects at risk of developing Crohn's disease.

D) Claim 24-27, 33, 39 are indefinite because the claim fails to provide any particular method for determining whether the patient's risk is increased, neutral or decreased. It is unclear which software program would allow for the prediction of a patient's risk. Based upon the teachings, the specification appears to contemplate delivering the results from the wet assay via the computer or via the internet. The specification does not appear to have any software for calculating risks. Thus, it is unclear whether the calculating the patient's risk is a number value, or a yes/no answer to increased risk. Thus, the metes and bounds of the claimed invention are unclear.

Conclusion

8. No claims allowable.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (571) 272-0743. The examiner can normally be reached Monday-Friday from 8:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272-0745.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

J. Goldberg

Jeanine Goldberg
Patent Examiner
April 19, 2004